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ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/817,905	Hausch
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 9, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 1, 13, 20, and 24-26 have been amended.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 1-20, 25-27, and 29-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Fu et al. (U.S. Patent 6,436,635 B1) (August 20, 2002).

Fu et al. teaches a method for the analysis of a sample of genetic material for detailed sequence information contained in a large set of distinct sequences of the sample (the "target sequences") (Abstract), comprising the following steps:

(1) producing an amount of nucleic acid templates containing the target sequences by multiplexed amplification of the sample of genetic material (Column 26, lines 1-17);

(2) using a chip with spatially separated locations containing a photocleavable oligonucleotide probe each for each target sequence to be investigated, the probes covalently bound to the chip surface (Abstract, Examples 2-9 and Claims 1 and 32);

(3) modifying in a single reaction vessel and by using the templates produced in step (1), all oligonucleotide probes on the chip synchronously in a template-dependent manner so that the information under investigation is transferred from the target sequences of the templates to the probes (Examples 11 and 12),

(4) cleaving and mass spectrometrically measuring the spatially separated probes (Examples 12, 14 and 15 and Claims 38 and 39), and

(5) extracting the detailed sequence information from the mass measurements of the probes (Examples 12, 14 and 15 and Figures 14-16 and Claims 40 and 41).

Fu et al. teaches the method, wherein the mass of the probes is measured in a time-of-flight mass spectrometer by ionization through laser desorption pulses (Column 18, lines 35-47 and Claim 41).

Fu et al. teaches the method, wherein the target sequences are amplified before analysis in a single-vessel reaction (Column 26, lines 1-17).

Fu et al. teaches the method, wherein the immobilized probes on the solid substrate are purified by from contaminations and released from the template nucleic acid by intensive and, if necessary, denaturing washing after modification (Figure 10, second and third step).

Fu et al. teaches the method, wherein the probes are released from the solid substrate by irradiation after modification and purification and thereby are made accessible for mass spectrometric analysis (Column 17, line 64 to Column 18, line 47).

Fu et al. teaches the method, wherein the photolytic cleavage of the oligonucleotide probes from the solid substrate surface occurs simultaneously with their desorption and ionization in the laser desorption analysis (Column 18, line 48 to Column 19, line 22).

Fu et al. teaches the method, wherein mass spectrometric detection is performed by MALDI-TOF (Column 19, line 46 to Column 20, line 2).

Fu et al. teaches the method, wherein the probes are immobilized on a surface suitable for MALDI-TOF spectrometry, the modification of the probes occurs at this surface, and the photolytic release occurs during the MALDI-TOF measurement (Column 17, line 21 to Column 20, line 24).

Fu et al. teaches the method, wherein the modification of the photocleavable probes occurs by a template-dependent primer elongation (Examples 11 and 12).

Fu et al. teaches the method, wherein at least one dideoxynucleotide is inserted during the template-dependent primer elongation of the photoclevable probes (Example 12).

Fu et al. teaches the method, wherein the modification of the photoclevable probes occurs by a template-dependent ligation using suitable reporter oligonucleotides (Example 12).

Fu et al. teaches the method, wherein the template specificity of the ligation is raised additionally by the sequence of the reporter oligonucleotide (Example 12).

Fu et al. teaches the method, wherein the insertion and deletion mutations are analyzed in particular by the addition template specificity of the reporter oligonucleotides (example 9).

Fu et al. teaches the method, wherein the reporter oligonucleotides can carry an additional recognition group consisting of a mass or affinity marker (Table 6, Figure 12 and Examples 7 and 9 and Examples 18-20).

Fu et al. teaches the method, wherein the modification of the photocleavable probe is performed by a template-dependent, endonucleolytic cleavage or restriction enzyme using single-strand specific nucleases (Column 17, lines 57-60 and Example 1).

Fu et al. teaches the method, wherein single strand mismatches of hybridizations between probes and target sequences can be identified by template-dependent nuclease digests of the photocleavable probes (Example 1 and Column 17, line 50 to Column 18, line 3).

Fu et al. teaches the method, wherein the hybridization of the target sequences to the photocleavable oligonucleotide probes and their template-dependent modification can be performed cyclicly a number of times (Examples 9-12).

Fu et al. teaches the method, wherein the enzymes used are heat stable and the reaction mixture can be repeatedly warmed directly on the chip (Examples 10 and 11).

Fu et al. teaches the method, wherein the chip carries, on its surface, 10 to 100,000 spatially separated, photocleavable oligonucleotide probes (Claims 32-39 and Example 9, Table 7 and 9).

Fu et al. teaches the method, wherein the photocleavable oligonucleotide probe is connected additionally with a functional group consisting of amino, sulfhydryl, carboxyl group, biotin, to the surface via a spacer in such a way that the enzymatic modification of the probe is facilitated (Column 15, line 12 to Column 16, line 21).

Fu et al. teaches the method, wherein the probes are immobilized in an array format on the surface of the chip as photocleavable oligonucleotide conjugates (Column 14, line 15 to Column 15, line 58).

Fu et al. teaches the method, wherein the photocleavable oligonucleotide probe is synthesized directly in unison on the surface and then if necessary the spacers are synthesized (Column 14, line 15 to Column 16, line 21).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 21- 24 are rejected under 35 U.S.C. 103(a) over Fu et al. (U.S. Patent 6,436,635 B1) (August 20, 2002) in view of Chee et al. (U.S. Patent 6,355,431 B1) (March 12, 2002).

Fu et al. teach the method of claims 1-20, 25-27, and 29-34 as described above.

Fu et al do not teach the method, wherein the endonucleolytic cleavage occurs using double strand-specific nuclease RNAseH when there is perfect base pairing, leading to detection of mismatch and the oligonucleotide probe contains at least one ribonucleotide.

Chee et al. teach the method, wherein the endonucleolytic cleavage occurs using double strand-specific nuclease RNAseH when there is perfect base pairing, leading to detection of mismatch and the oligonucleotide probe contains at least one ribonucleotide (Column 26, lines 15-22).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the endonucleolytic cleavage occurs using double strand-specific nuclease RNAseH when there is perfect base pairing,

leading to detection of mismatch and the oligonucleotide probe contains at least one ribonucleotide of Chee et al. in the method of Fu et al. since Chee et al. states, "The nicking is facilitated especially when carried out with a double stranded ribonuclease such as RNAseH or Exo III. RNA probes made entirely of RNA sequences are particularly useful because first, they can be more easily produced enzymatically, and second, they have more cleavage sites which are accessible to nicking or cleaving by a nicking agent such as the ribonucleases (Column 26, lines 15-22)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the method, wherein the endonucleolytic cleavage occurs using double strand-specific nuclease RNAseH when there is perfect base pairing, leading to detection of mismatch and the oligonucleotide probe contains at least one ribonucleotide of Chee et al. in the method of Fu et al.., in order to improve the analysis of a target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method, wherein the endonucleolytic cleavage occurs using double strand-specific nuclease RNAseH when there is perfect base pairing, leading to detection of mismatch and the oligonucleotide probe contains at least one ribonucleotide of Chee et al. in the method of Fu et al., in order to achieve the express advantages noted by Chee et al., of an invention that provides RNA probes made entirely of RNA sequences which are particularly useful because first, they can be more easily produced enzymatically, and second, they have more cleavage sites which are accessible to nicking or cleaving by a nicking agent such as the ribonucleases such as RNAseH.

6. Claim 28 is rejected under 35 U.S.C. 103(a) over Fu et al. (U.S. Patent 6,436,635 B1) (August 20, 2002) in view of Southern et al. (U.S. Patent 6,307,039 B1) (October 23, 2001).

Fu et al. teach the method of claims 1-20, 25-27, and 29-34 as described above.

Fu et al do not teach the method, wherein the photocleavage site consists of an 0-nitrobenzyl residue.

Southern et al. teach the method, wherein the photocleavage site consists of an 0-nitrobenzyl residue. (Example 6, Column 10, lines 40-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the photocleavage site consists of an 0-nitrobenzyl residue. of Southern et al. in the method of Fu et al. since Southern et al. states, "The NB group has also been shown to be removable by uv light to leave a fully functional phosphate group (Column 10, lines 54-56)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the method, wherein the photocleavage site consists of an 0-nitrobenzyl residue. of Southern et al. in the method of Fu et al. , in order to improve the analysis of a target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method, wherein the photocleavage site consists of an 0-nitrobenzyl residue. of Southern et al. in the method of Fu et al. , in order to achieve the express advantages noted by Southern et al., of an invention that provides the photocleavable 0-nitrobenzoyl derivative NB group which has also been shown to be removable by uv light to leave a fully functional phosphate group.

Response to Amendment

7. In response to amendment, 112(second paragraph) rejections have been withdrawn. However, 102(e) and other 103(a) rejections are hereby properly maintained.

Response to Arguments

8. Applicant's arguments filed on April 9, 2003 have been fully considered but they are not persuasive.

Applicant argues (Page 3, fourth paragraph to page 4, third paragraph) that 102(e) rejection should be withdrawn because Fu et al. (U.S. Patent 6,436,635 B1) (August 20, 2002) does not teach or suggest the main feature of the claimed invention i.e., the use of covalent bonds for immobilization of the probes which are cleavable using photocleavage. This argument is not persuasive. Fu et al clearly teaches the use of covalent bonds for immobilization of the probes which are cleavable using photocleavage, as Fu et al teaches, "Nucleic acids may be attached to the solid support by a photocleavable bond, an electrostatic bond, a disulfide bond, a peptide bond, a diester bond or a **combination of these sorts of bonds**" (Column 17, lines 30-33). The combination of a photocleavable bond with a disulfide bond, a peptide bond, or a diester bond (which are covalent bonds), as explicitly taught by Fu et al., clearly anticipates the claimed invention.

Applicant did not argue or comment extensively on the content of Chee reference and Southern reference, which are the basis of 103(a) rejections.

In response to arguments, all previous 102(e) as well as 103(a) rejections are hereby properly maintained.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to

Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

May 21, 2003

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